

OTHER CONSTITUENTS

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## I. INTRODUCTION

The following is a brief discussion of other constituents in cigarette smoke sometimes referenced by anti-smokers. As stated previously, the vast majority of such constituents, some of which have been identified in "tar," are present in cigarette smoke only in extremely small amounts. As is the case with "tar," nicotine and CO, these minute subfractions of tobacco smoke have not been scientifically proven to cause human disease as they are encountered by the smoker.

## II. OTHER CONSTITUENTS

### Acetaldehyde

Acetaldehyde is reportedly present in cigarette smoke in minute quantities. It is a chemical compound related to ethanol and is used in the manufacturer of plastics and synthetic rubber. Acetaldehyde is also commonly found in perfume.<sup>1</sup> Exposure to extremely high levels of acetaldehyde has an eye and skin irritant effect, and may be toxic.<sup>2</sup> However, an international research group recently concluded that the data was "inadequate" to support any claim that acetaldehyde causes cancer in humans at any level of exposure.<sup>3</sup>

### Acetone

Acetone has been reported to be present in minute quantities in the "vapor phase" of cigarette smoke, i.e., it is not found in "tar" (smoke condensate). It is most commonly encountered either at work or at home in the form of cleaning solvent. It has

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also been detected in freeze-dried foods and dried milk. Moreover, acetone is a naturally occurring constituent of human blood and urine.<sup>4</sup>

Acetone is not considered toxic at low levels of exposure, although at higher levels of exposure it can be an eye or skin irritant.<sup>5</sup> One researcher reported that he was unable to produce tumors through the mouse-skin painting method using acetone.<sup>6</sup>

#### Acrolein

Acrolein has been reported to be present in small quantities in the vapor phase of cigarette smoke. It is also everywhere in the environment as a product of fires, automobile exhaust, and other industrial emissions. Acrolein is also produced by burning foods containing fat, such as grilling a steak.<sup>7</sup> Although at high concentrations acrolein may have a toxic or irritant effect, one recent review of the research conducted regarding acrolein's toxicity or carcinogenicity in humans concluded "there is no evidence to support that acrolein is a human carcinogen."<sup>8</sup>

#### Ammonia

Ammonia is reportedly detectable in minute amounts in cigarette smoke. It occurs naturally as a part of protein metabolism in man and in virtually all species of animals. Ammonia is widely used as a fertilizer. It is also a common household cleanser.<sup>9</sup> At high concentrations, ammonia can have a strong irritant

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effect and cause burns; its pungent odor, of course, is very familiar. One researcher, however, recently noted that:

The biologic significance of inhaled ammonia in the concentrations generated in mainstream smoke, which are very low, is purely conjectural.<sup>10</sup>

#### Arsenic

Arsenic is a naturally occurring metal that is drawn into growing tobacco (and other plants) from the soil. It is present also in rocks, water, and virtually all living organisms in concentrations of parts per million and parts per billion. The United States government has estimated that non-smokers generally take in up to 60 micrograms of arsenic per day from various sources; it has also estimated that smokers take in an additional two micrograms of arsenic per pack of cigarettes smoked, thus increasing their daily arsenic intake only marginally.<sup>11</sup> One recent literature review noted that over 99% of the arsenic (and other metals such as lead and cadmium) in tobacco remains in cigarette ash.<sup>12</sup>

Analyses of the literature regarding the relationship between exposure to arsenic and disease have generally been inconclusive. For example, in a recent review of the literature, a researcher characterized "its claimed effects on human smokers as speculative."<sup>13</sup> The 1982 U.S. Surgeon General's Report also noted that "the view that inorganic arsenicals cause cancer of the skin and lung has not been widely accepted. . . ."<sup>14</sup>

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### Benzene

Benzene has been reported to be present in the vapor phase of cigarette smoke in small quantities. Although benzene has sometimes been suggested as a possible cause of leukemia, leukemia has not been consistently related to cigarette smoking in the various statistical studies that form the primary basis for public health criticism of smoking.<sup>15</sup> The U.S. Surgeon General has also noted that "no dose-response relationship has been established between death rate from leukemia and number of cigarettes smoked."<sup>16</sup>

### Benzo(a)pyrene

Benzo(a)pyrene (BaP) is sometimes singled out as a possible human carcinogen because it is a component of the laboratory product "tar;" "tar," as noted above, can produce tumors under the highly artificial conditions involved in animal skin painting experiments. Claims that BaP, and other polycyclic aromatic hydrocarbons (such as dibenzacridine), can cause cancer in humans thus suffer from the same weaknesses as those claims generally directed at "tar."

BaP is formed by the incomplete combustion of organic matter. In addition to cigarette smoke, other sources of BaP in the atmosphere are coal and oil fired power stations, domestic heating, industrial processes and emissions, automobile emissions, and forest fires and volcanic activity. Atmospheric BaP is carried into the soil, the water table, and the ocean through rainfall. Thus, BaP is detectable in fish, meat and vegetables, as well as

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in drinking water. Foodstuffs as varied as coconut oil, sardines, and cheese all contain BaP at relatively high levels. Charcoal-grilled meats have been reported to contain particularly high levels of BaP.<sup>17</sup> Two researchers concluded that the BaP concentration in a single charcoal-grilled steak was equivalent to that in the smoke of 600 cigarettes.<sup>18</sup> The daily levels of exposure to BaP simply from breathing the air in some cities has been estimated, by a former U.S. Surgeon General, to be approximately twice as high as that for a cigarette smoker.<sup>19</sup>

#### Butane

Butane may be present in the vapor phase of cigarette smoke in minute quantities. It occurs in natural gas and is present in the atmosphere as the result of the combustion of gasoline and other petroleum products. Butane is also frequently used as an aerosol propellant. The inhalation of butane has not been demonstrated to produce disease in humans.<sup>20</sup>

#### Cadmium

Cadmium is a trace "heavy metal" that has been reported to be present in tobacco and in cigarette smoke in certain compound forms. It is used extensively in the production of cadmium-copper alloys and corrosion-resistant coatings. It is found in alkaline batteries, glass, solder, paint pigments and some pesticides and fungicides. The principal sources of cadmium exposure for man are in food, dairy products and drinking water.<sup>21</sup>

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It has been estimated that in most countries the average smoker is exposed to approximately the same amount of cadmium daily through smoking as he or she is through diet.<sup>22</sup> Other researchers recently concluded that the amount of cadmium in two packs of cigarettes, even if entirely inhaled, would still be less than would be inspired in two hours of breathing atmospheric cadmium at the maximum safe levels established by the health authorities of several countries.<sup>23</sup>

Cadmium has been identified as a possible tumor promotor under experimental conditions in animals. Three German researchers recently observed, however, that the results of these experiments should not be extrapolated to humans because the doses necessary to induce tumor production corresponded to smoking between 5,000 to 20,000 cigarettes per day.<sup>24</sup> Similarly, a recent review of the literature concerning the claimed carcinogenicity of cadmium noted that "evidence for potential cadmium carcinogenicity in humans in the dosages delivered from smoking is very limited."<sup>25</sup>

#### Chromium

Chromium is a metal that is reportedly detectable in trace amounts in tobacco. Like the other trace metals in tobacco, it is drawn into the growing plant from the soil. Also like the other metals in tobacco, it is estimated by one researcher that over 99% of the chromium in tobacco remains in cigarette ash and is not transferred into smoke.<sup>26</sup> A group of researchers recently concluded that "[t]here is no indication . . . that the chromium

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[in tobacco] goes to the mainstream smoke."<sup>27</sup> (Emphasis added)

Chromium is a naturally occurring element of rock; as rock is weathered into soil, the chromium is transferred into the soil as well. From the soil, chromium is both washed into the oceans, where it is incorporated into the oceanic food-chain, and it is taken up by growing plants and incorporated into the land food-chain. Chromium compounds are also present in the atmosphere as a result of industrial emissions of the burning of organic matter.<sup>28</sup> Food is the principal environmental source of chromium intake by man, with vegetables, unrefined sugar, beef, liver, eggs and animal fats generally having the highest concentrations.<sup>29</sup>

Studies of various illnesses developed by workers in the chromate industry, who were exposed to large concentrations of chromium compounds over many years, have raised concerns about chromium as a possible cause of chronic disease in humans.<sup>30</sup> These studies have been subject to scientific criticism.<sup>31</sup> Given the extremely low level, if any, to which a smoker is exposed to chromium beyond his or her normal dietary and environmental chromium intake, according to one researcher "its role as a potential carcinogen in human smokers is not known."<sup>32</sup>

#### Hydrogen Cyanide

Hydrogen cyanide (HCN) is also reportedly present in minute amounts in the vapor phase of cigarette smoke. It is produced by the combustion of the amino acids in tobacco. HCN is also generated by the combustion of carbon materials in air, for

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example, during home cooking. HCN is used in a variety of industrial processes and is also present in such varied food products as bitter almonds, lima beans, soybeans, apricots, and linseed. It has been detected in certain wines.<sup>33</sup>

A recent study noted that although the HCN level detectable in smokers' blood is slightly elevated after smoking, it is rapidly eliminated from the system.<sup>34</sup> Another reviewer concluded that the effect of HCN in cigarette smoke, if any, on humans "remains to be determined."<sup>35</sup>

#### Lead

Lead, like the other trace metals reportedly present in tobacco, is drawn from the soil into the growing plant. Also like the other trace metals, one researcher estimated that less than one percent of the lead in the tobacco is transferred to the smoke, with the remainder left in the ash.<sup>36</sup> Lead is present in the air, soil and water. Hence, smokers and non-smokers alike are exposed to and ingest small amounts of lead each day. One research group has estimated that a smoker will ingest five micrograms of lead from a pack of cigarettes; the dietary intake of lead per day, however, has been reported to be much higher.<sup>37</sup>

Numerous health concerns have been expressed regarding exposure to high levels of lead and lead compounds. However, given the very low levels of lead exposure from tobacco, one researcher concluded that "the role of lead as a potential carcinogen for human smokers is not known."<sup>38</sup>

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### Methanol

Methanol is reported to be present in very small quantities in cigarette smoke as a vapor phase component. It is used in enamels, dyes, stains, cleaning solvents, paint and varnish removers, antifreeze mixtures, and as fuel for internal combustion engines. It is also present in bread, soy sauce and various fruits and vegetables.<sup>39</sup>

Methanol can be a skin and eye irritant in large concentrations. One researcher recently noted, however, that "[c]onsidering the dose of methanol estimated to be toxic to humans (1 g/kg), it is unlikely that a normal human being could ever be exposed to enough of it by inhalation to experience acute toxicity."<sup>40</sup> This scientist also noted that he had been unable to find any studies showing the inhalation of methanol to be carcinogenic.

### Naphthalene

Naphthalene is a substance related to benzene. It is reportedly present both in "tar" and in the vapor phase of cigarette smoke in small quantities, and is generated by the combustion of tobacco. Naphthalene is used extensively in the chemical, plastics and dye industries. In the home, it is found frequently in air fresheners, moth balls, varnishes and wood preservatives. Radishes also contain naphthalene.<sup>41</sup> Naphthalene has no conclusive reported carcinogenic effect, although it is sometimes associated with leu-

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kemia in animal experiments. As noted above, leukemia has not been consistently statistically associated with cigarette smoking.<sup>42</sup>

### Nickel

Nickel, like arsenic, is drawn from the soil into growing tobacco. Also like arsenic, it is estimated that 99% of the nickel in tobacco remains in the ash of a cigarette, and is not transferred to the smoke. The U.S. Surgeon General has concluded that "it is not likely that nickel plays a significant role in the etiology of lung cancer in cigarette smokers. . . ."<sup>43</sup> Other researchers and reviewers have reached the same conclusion.<sup>44</sup>

### Nitrogen Oxides

Cigarette smoke reportedly contains nitric oxide (NO), but "very little, if any," nitrous oxide or nitrogen dioxide.<sup>45</sup> The U.S. Surgeon General has noted data showing that both smokers and nonsmokers maintain "a consistently low level" of NO in their blood and has suggested that the "lack of a significant difference" between the two groups indicates that NO from external sources "appears to have little effect" on the amount found in the blood.<sup>46</sup>

### Nitrosamines

Nitrosamines reportedly are detectable in both "tar" and in the vapor phase component of cigarette smoke. The presence of nitrosamines in cigarette smoke is often the subject of public comment by anti-smoking advocates because, under experimental con-

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ditions, certain nitrosamine compounds can produce tumors in laboratory animals. As two reviewers of the literature noted, however, "direct epidemiologic evidence that would associate nitrosamines with human cancer is very limited."<sup>47</sup> Another recent reviewer suggested that:

The role of nitrosamines in the pathogenesis of human lung cancers is theoretical, and it is yet to be shown conclusively that any specific N-nitroso compound causes human cancer.<sup>48</sup>

Even the U.S. Surgeon General has stated that there is "a lack of direct evidence" that the nitrosamines specific to tobacco have any proven health effect on smokers.<sup>49</sup>

The components of nitrosamines -- nitrates, nitrites and amines -- are naturally occurring substances. Hence, nitrosamines are found in soil, air, water and food. Beer and scotch whiskey have recently been determined to contain dimethylnitrosamine.<sup>50</sup> Foods often prepared with nitrites (used as a preservative) include ham, sausages, bacon, luncheon meats and frankfurters; seafood and cheese also often contain nitrosamines.<sup>51</sup>

#### Phenol

Phenol is reported to be present in minute quantities in cigarette smoke and is detectable in "tar." It has a variety of industrial uses, including the manufacture of perfumes, plastics and fertilizers. Phenol occurs naturally in animal tissues; the consumption of meat has been identified as the primary source of human exposure to phenol. It is also present in drinking water.<sup>52</sup>

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Two reviewers of the literature concluded that "[t]here is no specific evidence of human cancer attributable to phenol or related compounds. . . ."<sup>53</sup> A group of researchers likewise reported that phenol is not present in cigarette smoke at high enough concentrations to cause disease in smokers.<sup>54</sup>

#### Polonium-210

Polonium-210 is a radioactive element that has been reported to be present in trace amounts in tobacco and cigarette smoke. It is also present in the atmosphere and in soil -- both as a part of the earth's natural background radiation and as a result of nuclear testing -- from which it is presumably drawn into growing tobacco. Smoking critics often cite the presence of polonium-210 in smoke as significant because it, along with most other radioactive materials, can have adverse health effects in humans and in animals if the exposure is of sufficient intensity. Even the U.S. Surgeon General, however, has questioned the significance of polonium-210 to lung cancer in humans.<sup>55</sup> Other researchers have disputed the conclusion drawn by some scientists that polonium-210 accumulates in the lung tissue of smokers.<sup>56</sup> Additional researchers discount the claimed risk to smokers of inhaled polonium, noting the extraordinarily minute quantities at which it is present.<sup>57</sup>

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### Toluene

Toluene is reported to be a constituent of the vapor phase component of cigarette smoke. It is present in the atmosphere as a result of industrial emissions, automobile emissions, and gasoline evaporation. Exposures at home include inks, dyes, and perfumes.<sup>58</sup> Although it is an eye and skin irritant at low levels and concentrations, toluene has not been reported to be toxic or to cause chronic disease in humans at those levels.<sup>59</sup>

### Urethane

Urethane (ethyl carbamate) has been reported to be present in cigarette smoke in very small amounts. It has been widely used in the plastics and textile industries. It is also used in a variety of agricultural chemicals, pesticides, fungicides, and in some therapeutic drugs. Urethane is a natural by-product of fermentation, and is found in wines, distilled spirits, and beer, as well as in fermented food products such as cheese, yogurt and soy sauce.<sup>60</sup> The U.S. Surgeon General has conceded that urethane, although possibly an animal carcinogen, is not present in cigarette smoke in sufficient quantities to cause cancer in smokers.<sup>61</sup>

### Vinyl Chloride

Vinyl chloride is reportedly present in minute amounts in the vapor phase of cigarette smoke. Although it is a gas, it is detectable in various food products such as honey, butter and tomato ketchup. It is also present in some wines.<sup>62</sup> Vinyl chloride

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is also used in the manufacture of plastics.<sup>63</sup>

Vinyl chloride has been reported to have toxic and carcinogenic effects in animals at high concentrations; a similar effect on humans has been suggested. One group of oncologists, however, although subscribing to the general theory that smoking causes cancer, conceded that:

Based on human data and results from animal studies, it appears to us that the[] minute amounts of [vinyl chloride in cigarette smoke] will not contribute to a measurable degree<sup>64</sup> to the carcinogenic activity of tobacco smoke.

This conclusion was echoed by a recent literature reviewer, who concluded that vinyl chloride is present in cigarette smoke "apparently at levels too low to be considered a carcinogen or fibrosis-inducing agent."<sup>65</sup>

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TOBACCO SMOKE CONSTITUENTS

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## I. INTRODUCTION

Tobacco smoke is a highly complex mixture containing, by some estimates, over 4,000 constituents. Over the years, much time and effort has been devoted to determining the identity of tobacco smoke constituents. This has proven difficult, however, and much remains to be learned about the structure and makeup of tobacco smoke and its relationship, if any, to human disease.

Ninety percent of cigarette smoke is air, water and carbon dioxide, a natural by-product of combustion. Of the remaining 10 percent, only a few substances such as nicotine and carbon monoxide (CO) have been measured by researchers as being present in smoke at levels above one milligram per cigarette. Anti-smoking advocates frequently assert that nicotine and CO cause disease in humans. The same is also said about "tar," even though it is a laboratory product, not an actual constituent of tobacco smoke.

The vast majority of the remaining constituents actually present in cigarette smoke, some of which have been identified in "tar," are present only in extremely small amounts, measured in micrograms (millionths of a gram) or nanograms (billionths of a gram) per cigarette. Nonetheless, anti-smoking advocates occasionally single out for public criticism certain smoke constituents other than "tar," nicotine and CO that have, under conditions and at levels vastly different from those to which a human smoker is

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exposed, been associated with disease in animals or humans. These substances, however, are ubiquitous. Smokers and non-smokers alike are exposed to most of these substances every day simply by breathing air, drinking water and eating food.

The significance of smoke constituents to human health, if any, is not yet understood. According to one researcher in the area, "no ingredient [constituent] or group of ingredients [constituents] as found in tobacco smoke have been established as disease producing in smokers."<sup>1</sup>

## II. SMOKE CONSTITUENTS

### A. "Tar"

"Tar" is an artificially created laboratory product consisting of highly concentrated and physically altered cigarette smoke particulate matter which is gathered either by passing cigarette smoke through a cold trap at extremely low temperatures or by using filters and a drying process. The substances as found in "tar" are not found in cigarette smoke. That may be why this product is sometimes referred to as condensate. Certainly, material collected in this way does not duplicate what humans are exposed to when they smoke. As a report on a meeting of experts in the area noted:

[T]here is, at present, no available instrumentation permitting the separation and

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individual collection of the particulate and gas phases which duplicates the precise physico-chemical conditions prevailing in cigarette smoke as it is inhaled.<sup>2</sup>

Despite its apparent lack of relevance to smoking, laboratory-produced "tar" has been used in animal experiments designed to investigate the possible relationship between tobacco smoke and cancer. In those experiments, "tar" was repeatedly painted on the shaved backs or ears of test animals over prolonged periods of time. These so-called skin-painting experiments have prompted a great deal of interest, as the tumors which resulted have been said to be evidence that tumors might develop in human lungs from inhaling cigarette smoke.

The results of such animal experiments cannot and should not be extrapolated to the human situation. Even if the "tar" collected by the methods described above were present in cigarette smoke, the "tar" used in skin painting experiments is very different by the time it is studied in the laboratory. That is because after "tar" is collected, it continues to undergo chemical changes as long as it is stored.<sup>3</sup> Furthermore, as an experimental toxicologist has noted, even if an effect such as tumor production is observed in a particular species, that does not necessarily mean that it might "occur either quantitatively or qualitatively in man."<sup>4</sup>

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Skin painting experiments suffer from a number of additional weaknesses. For example, the concentrations of "tar" used in such experiments are extremely high. It has been estimated that the amounts utilized would be equivalent to an individual smoking over 100,000 cigarettes per day.<sup>5</sup> Furthermore, the skin and ears of laboratory animals are not similar to human lung tissue. Animal skin lacks the intricate clearance mechanisms of the lungs, such as the mucus blanket which coats the lining of the major airways of the lung. Even the summary report of a study sponsored by the United States government utilizing skin painting techniques conceded "the uncertain relationship between tumors resulting from mouse skin painted with condensate and human lung cancer."<sup>6</sup> Consequently, such experiments have been characterized as involving applying "the wrong material in the wrong form, in the wrong dosage, to the wrong tissue of the wrong animal."<sup>7</sup>

It is misleading, therefore, to draw definitive conclusions about "tar" and human disease from skin painting studies. As a knowledgeable observer of research in this area has stated: "Bronchogenic carcinoma [lung cancer] has never been produced by tobacco or its products in any experimental animal despite the multiplicity of attempts."<sup>8</sup> (Emphasis added) All in all, the following statement made in the mid-1970's still provides a concise summary of the current state of scientific data concerning "tar":

Human beings do not smoke 'tar' and laboratory reports on 'tar' yields have not been established as significant to human health.

B. Nicotine

Nicotine is a natural element of tobacco and, thus, is present in tobacco smoke. Nicotine has been described by some researchers as having no known chronic or cumulative effects on human health.<sup>10</sup> The data on the nature of nicotine's relationship to human health is inconclusive at best, because, among other things, science cannot determine with any precision how much nicotine a smoker is exposed to. In fact, no correlation between the nicotine level of a cigarette or the number of cigarettes smoked and the smoker's actual nicotine intake has been conclusively established because of individual variations in puff rates, depth of inhalation, and body metabolism.<sup>11</sup>

Nonetheless, anti-smoking advocates blame nicotine for the development of heart disease. Yet no biological mechanism by which nicotine, or any other agent, may be involved in heart disease has been demonstrated. Serious questions about what role, if any, nicotine plays have been raised as a result of autopsy findings of fatty deposits and other changes in the arteries of individuals who either have not smoked or could have smoked only briefly, such as infants, children, and young men killed in military battle.<sup>12</sup> Even the 1983 U.S. Surgeon General's Report, which focused on car-

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diovascular disease, concedes that "the evidence for and against a primary role for nicotine in the development or acceleration of atherosclerosis is not conclusive. . . ."<sup>13</sup> That opinion was shared by a German researcher who has conducted research on the relationship between nicotine and the clogging of arteries. After reviewing the literature, he and his co-author concluded that "there is no established evidence which supports the hypothesis that nicotine has any influence on the development" of those changes.<sup>14</sup> (Emphasis added)

Claims by anti-smoking advocates regarding the role of nicotine in the development of heart disease are further undermined by two epidemiological (population) studies. In a study that dealt with myocardial infarction (heart attack), the authors reported finding -- contrary to what they expected -- that the nicotine and carbon monoxide levels of the cigarettes their subjects smoked were not related to the risk of heart attack.<sup>15</sup>

The second study, chaired by a well-known British scientist opposed to cigarette smoking, examined the serum (blood) levels of cotinine, a nicotine metabolite, in male nonsmokers and smokers of cigarettes only, cigars only, and pipes only. The study determined that the mean cotinine level for pipe smokers was significantly higher than the levels for cigarette and cigar smokers. Since studies of pipe smokers generally have not reported an increased risk of coronary heart disease, the researchers concluded

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that "nicotine is unlikely to be the major cause of the excess coronary heart disease mortality in cigarette smokers."<sup>16</sup> After re-evaluating their methodology in response to anti-smoking criticism of their study, the researchers again concluded that they were "reasonably confident" that "exposure to high systemic concentrations of nicotine is not a cause of the disease." Although the researchers quibbled with the result of their own study, arguing that their data "cannot completely exonerate" nicotine, they added that the data do "substantially reduce the weight of evidence suggesting that nicotine is a cause of coronary heart disease."<sup>17</sup>

Animal studies which purport to establish a causal role for nicotine in heart disease have been soundly criticized for their unrealistic and excessive test conditions. An American researcher who conducted animal studies on this subject has noted:

There have been some studies that have exhibited minor or questionable changes with the use of an equivalent dose of 600 or more cigarettes a day in man. This is such a large number that I think man would find it difficult to find the time to smoke them.<sup>18</sup>

In contrast, this researcher concluded that animal studies using realistic doses of nicotine have "failed to initiate, exacerbate, or otherwise influence" the process leading to the clogging of arteries in test animals.<sup>19</sup> In one such study, which was funded by the United States government, male beagle dogs fed a special diet to induce this process were exposed for two years to cigarette

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smoke containing low or high levels of nicotine and, in some cases, enriched with carbon monoxide. According to the final report of the research laboratory which conducted the study, "the results of this study lent no support to the suggestion that cigarette smoking increases the rate of development" of this process.<sup>20</sup>

The foregoing demonstrates the validity of one researcher's summary: "While many studies have been done in this field, none have established nicotine as contributing to the causation, aggravation or precipitation of any cardiovascular disease."<sup>21</sup> (Emphasis added)

C. Carbon Monoxide

Carbon monoxide (CO) is a tasteless, odorless, colorless gas produced by many natural and man-made sources, including automobile exhaust and industrial emissions. It is naturally produced by the body during daily metabolism. Burning cigarettes also produce CO, but that amount has been described as "insignificant"<sup>22</sup> compared to most other sources. Nonetheless, CO has received considerable attention in the scientific literature, usually in regard to cardiovascular disease (CVD). In a review of such literature, however, two public health specialists concluded that "despite the large amount of literature available, the conclusions that can be drawn as to the role of CO in human CVD remain tentative and open to varying interpretations."<sup>23</sup> This conclusion is supported

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by a similar statement in the 1983 U.S. Surgeon General's Report, which focused on heart disease:

Carbon monoxide is another major component of cigarette smoke for which there are some data supporting a possible atherogenic [plaque forming inside the arteries] role; however, a review of recent literature on the role of carbon monoxide in arterial <sup>injury</sup><sup>24</sup> and atherosclerosis leads to no consensus.

The conclusion of another group which also reviewed the literature was more concise. The chairman of the American Heart Association Task Force on Environment and the Cardiovascular System reported that his group had concluded that the question of whether CO causes heart disease "remains unanswered even at the basic science level."<sup>25</sup> (Emphasis added)

Specialists who reviewed these and other studies have concluded that "there is no evidence" to support the suggestion that exposure to low or moderate levels of CO increases the rate of development of atherosclerotic disease in man. Indeed, they contend that "sufficient evidence is available to support the conclusion that, in fact, CO is not of pathogenetic [disease causing] consequence in atherosclerotic disease."<sup>26</sup> (Emphasis added)

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D. Other Constituents\*

Over the years, the principal focus of the attention and concern of smoking critics has been on "tar," nicotine and CO. One researcher who has tried to establish a causal link between smoking and disease, however, concluded with reference to these substances that:

We assume that it is the tar which causes lung cancer, but we do not know this for certain.

Until now, we have implicated nicotine in the development of cardiovascular diseases, but we cannot prove this.

The same is true for CO.<sup>27</sup>

Thus, some anti-smoking advocates have attempted to shift public attention to the presence of other substances in cigarette smoke. These substances, as found in cigarette smoke (like "tar," nicotine, and CO), have not been scientifically proven to cause any disease in humans. Nonetheless, these constituents are of interest because at levels and under conditions of exposure greatly different than those encountered by the smoker, certain of these compounds may have a toxic effect on or may be associated with disease in animals or humans.

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\* A more detailed discussion of specific constituents appears in Appendix A to this paper.

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It is an axiom among toxicologists that any substance is toxic if the level of exposure is high enough and no substance is toxic if the level of exposure is low enough.<sup>28</sup> The amount of substances other than nicotine and CO in cigarette smoke is extremely low, measured in terms of micrograms and nanograms per cigarette. As previously noted, a microgram is one-millionth of a gram, the equivalent of one second in twelve days. A nanogram is one billionth of a gram, the equivalent of one second in thirty-two years.

Moreover, these substances are for the most part natural by-products of combustion of any organic matter, including tobacco, or are found in any organic matter whether or not that matter is burned. Likewise, other compounds present in smoke are also present in the air we breathe and the water we drink. Thus, it is scientifically inaccurate to state as "fact" that there is something "unique" about the presence of these substances in cigarette smoke.

### III. CONCLUSION

Numerous claims have been made about the relationship between cigarette smoke constituents and the health of the smoker. However, such claims are just that -- claims which are not supported by reliable scientific proof. After years of study, no scientific relationship has been established between "tar," nicotine and carbon monoxide and human disease. Other constituents, detectable at extremely low levels in cigarette smoke, are the subject of occa-

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sional public comment. These substances are not unique to tobacco smoke, however, and as with "tar," nicotine and CO, have not been proven to cause disease in humans in the form in which they are found in cigarette smoke.

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